REMARKS/ARGUMENTS

The foregoing amendments in the specification and claims are of a formal nature, and do not add new matter. With this amendment, Claim 33 has been amended to further clarify what Applicants have always regarded as their invention.

Claims 33, 38-40 and 44-54 are pending after entry of the instant amendment.

Applicants note and appreciate the withdrawal of the earlier objections and rejections for double patenting and under 35 U.S.C. §112, second paragraph. The remaining rejections under 35 U.S.C. §101, 35 U.S.C. §112, first paragraph, and 35 U.S.C. §102 are addressed below.

I. Priority

The Examiner stated that the effective filing date for the application is December 12, 2001, the actual filing date of the present application, because the claimedpolynucleotides allegedly do not meet the requirements of 35 U.S.C. §112, first paragraph.

As previously stated in discussed in Applicants' response filed February 7, 2005, Applicants rely for patentable utility on the gene amplification assay (Example 143) which was first disclosed in U.S. Provisional Application Serial No. 60/162,506, filed October 29, 1999, priority to which has been claimed in this application. Applicants therefore respectfully maintain their position that the disclosure of the instant application, which is similar to that of the earlier-filed application (U.S. Provisional Application Serial No. 60/162,506, Example 20), provides the support required to establish utility for the claimed polynucleotides. Accordingly, Applicants submit that the subject matter of the instant claims is supported by the disclosure in U.S. Provisional Application Serial No. 60/162,506. Therefore, the effective filing date of this application is October 29, 1999, the filing date of U.S. Provisional Application Serial No. 60/162,506, and the present application is entitled to at least the October 29, 1999 priority for subject matter defined in Claims 33, 38-40 and 44-54.

II. Claim Objections

Claim 33 is objected to because of the recitation of the phrase "in of." Claim 33 has been amended herein to correct this typographical error.

The Examiner further states that the coding region should be designated via SEQ ID NO: residues, as the figure "only refers to bolding and underlining of start and stop codons and does not clarify the portion designated via the claim." (Pages 3-4 of the instant OfficeAction).

Applicants respectfully point out that Figure 31 clearly identifies the start and stop codons, shown in bold and underlined. This marking is clearly explained in the description of Figure 31 (page 286, lines 25-27). As the coding region of a gene is defined by the start and stop codons, one of skill in the art would immediately understand that the coding region of SEQ ID NO:53 is the sequence beginning with the start codon and ending with the stop codon. Accordingly, the meaning of the claim is clear, and the Examiner is respectfully requested to withdraw the objection.

III. Claim Rejections Under 35 U.S.C. §101 and 35 U.S.C. §112, First Paragraph

Claims 33, 38-40, and 44-54 stand rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well-established utility." (Page 4 of the instant Office Action). In particular, the Examiner asserts that "[t]he gene amplification assay is not noted to evidence specific and substantial asserted utility or well established utility because the noted expression is not prescribed to any reasonably likely indication." (Page 5 of the instant Office Action).

Claims 33, 38-40, and 44-54 are also rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement, because "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (Page 11 of the instant Office Action).

Applicants respectfully disagree and traverse the rejection.

Applicants submit, for the reasons set forth below, that the specification discloses at least one credible, substantial and specific asserted utility for the PRO1295 polynucleotide.

Utility – Legal Standard

According to 35 U.S.C. § 101:

> Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title. (Emphasis added.)

In interpreting the utility requirement, in *Brenner v. Manson*[1], the Supreme Court held that the quid pro quo contemplated by the U.S. Constitution between the public interest and the interest of the inventors required that a patent applicant disclose a "substantial utility" for his or her invention, *i.e.*, a utility "where specific benefit exists in currently available form."[2] The Court concluded that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. A patent system must be related to the world of commerce rather than the realm of philosophy."[3]

Later, in *Nelson v. Bowler*[4], the C.C.P.A. acknowledged that tests evidencing pharmacological activity of a compound may establish practical utility, even though they may not establish a specific therapeutic use. The court held that "since it is crucial to provide researchers with an incentive to disclose pharmaceutical activities in as many compounds as possible, we conclude adequate proof of any such activity constitutes a showing of practical utility."[5]

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[1] *Brenner v. Manson*, 383 U.S. 519, 148 U.S.P.Q. (BNA) 689 (1966).

[2] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

[3] *Id.* at 536, 148 U.S.P.Q. (BNA) at 696.

[4] *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (C.C.P.A. 1980).

[5] *Id.* at 856, 206 U.S.P.Q. (BNA) at 883.

In *Cross v. Iizuka*[6], the C.A.F.C. reaffirmed *Nelson* and added that *in vitro* results might be sufficient to support practical utility, explaining that "*in vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with the particular pharmacological activity are generally predictive of *in vivo* test results, i.e. there is a reasonable correlation there between."[7] The Court perceived "no insurmountable difficulty" in finding that, under appropriate circumstances, "*in vitro* testing, may establish a practical utility."[8]

The case law has also clearly established that applicants' statements of utility are usually sufficient, unless such statement of utility is unbelievable on its face.[9] The PTO has the initial burden that applicants' claims of usefulness are not believable on their face.[10] In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope."[11, 12]

Compliance with 35 U.S.C. §101 is a question of fact.[13] The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the

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[6] *Cross v. Iizuka*, 753 F.2d 1047, 224 U.S.P.Q. (BNA) 739 (Fed. Cir. 1985).

[7] *Id.* at 1050, 224 U.S.P.Q. (BNA) at 747.

[8] *Id.*

[9] *In re Gazave*, 379 F.2d 973, 154 U.S.P.Q. (BNA) 92 (C.C.P.A. 1967).

[10] *Ibid.*

[11] *In re Langer*, 503 F.2d 1380,1391, 183 U.S.P.Q. (BNA) 288, 297 (C.C.P.A. 1974).

[12] See also *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (C.C.P.A. 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (C.C.P.A. 1977).

[13] *Raytheon v. Roper*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984).

totality of the evidence under consideration.[14] Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

The well established case law is clearly reflected in the Utility Examination Guidelines ("Utility Guidelines")[15], which acknowledge that an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that are to be diagnosed.

In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a '"substantial" utility'."[16] Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement[17] gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular

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[14] *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d (BNA) 1443, 1444 (Fed. Cir. 1992).

[15] 66 Fed. Reg. 1092 (2001).

[16] M.P.E.P. §2107.01.

[17] M.P.E.P. §2107 II (B)(1).

practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Utility – Application of Standard

As discussed in the previous Response filed February 7, 2005, Applicants rely on the gene amplification data for priority and to establish patentable utility for the PRO1295 polynucleotide. The Examiner has acknowledged that the instant application discloses that the nucleic acid encoding the PRO1295 polypeptide is amplified in primary tumor cell lines including, lung, colon and breast. (See page 8 of the instant Office Action).

However, the Examiner alleges that "[o]ne skilled in the art would not conclude that such a correlation would indicate that PRO1295 is diagnostic or prognostic for lung, colon, or breast cancer because there is no indication that a majority of any particular cancer type or cancer cell in general exhibit gene amplification of PRO1295 in comparison to other similar and not dissimilar cell types." (Page 8 of the instant Office Action).

Applicants respectfully disagree.

Applicants respectfully submit that the specification discloses that the nucleic acids encoding PRO1295 had ΔCt value of > 1.0, which is a **more than 2-fold increase**, in at least 5 of the tumors listed in Table 8. The specification clearly discloses that that significant amplification of nucleic acid DNA59218-1559 encoding PRO1295 occurred (1) in primary lung tumors: HF-000631 and HF-000840; (2) colon tumor centers: HF-000539 and HF-000698; and (3) in breast tumor center HF-000545.

In addition, in the previous Response filed February 7, 2005, Applicants submitted the Declaration by Audrey Goddard, Ph.D. which clearly establishes that the TaqMan realtime PCR method described in Example 143 has gained wide recognition for its versatility, sensitivity and accuracy and is in extensive use for the study of gene amplification. Dr. Goddard in her Declaration confirms that an at least 2-fold increase in gene copy number in a tumor tissue sample relative to a normal (*i.e.*, non-tumor) is significant and useful. The Goddard Declaration further confirms that based on the gene amplification results set forth in Table 8, one of ordinary

skill would find it credible that a 2-fold increase in gene copy number (as seen with PRO1295) would indicate that the gene is a diagnostic marker of human lung or colon cancer.

The case law has clearly established that in considering affidavit evidence, the Examiner must consider all of the evidence of record anew.[18] "After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument"[19] Furthermore, the Federal Court of Appeals held in *In re Alton*, "We are aware of no reason why opinion evidence relating to a fact issue should not be considered by an examiner"[20]. Applicants also respectfully draw the Examiner's attention to the Utility Examination Guidelines[21] which states, "Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered." The statement in question from an expert in the field (the Goddard Declaration) states that "a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy." Therefore, barring evidence to the contrary regarding the above statement in the Goddard Declaration, this rejection is improper under both the case law and the Utility guidelines.

Further, Applicants respectfully submit that the amplification of the nucleic acids in even one lung, colon or breast tumor provides specific and substantial utility for the nucleic acid as a diagnostic marker of the type of lung, colon, or breast tumor in which it was amplified.

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[18] *In re Rinehart,* 531 F.2d 1084, 189 USPQ 143 (CCPA 1976) and *In re Piasecki,* 745 F 2d. 1015, 226 USPQ 881 (Fed. Cir. 1985).

[19] *In re Alton,* 37 USPQ2d 1578,1584 (Fed. Cir. 1996) (quoting *In re Oetiker,* 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992)).

[20] *In re Alton, supra.*

[21] Part IIB, 66 Fed. Reg. 1098 (2001).

Applicants submit that the tumors listed in Table 8 are not similar tumors from different patients, but various types/classes of lung/colon/breast tumors at different stages. Accordingly, a positive result from one tumor, where the nucleic acid was amplified, but not from other tumors, indicates that the nucleic acid can be used as a marker for diagnosing the presence of that kind of tumor in which it was amplified. Amplification of the nucleic acid would be indicative of that specific class of lung/colon/breast tumor, whereas absence of amplification would be non-conclusive.

The Examiner further asserts that Applicants' submitted references allegedly "fail to evidence that such noted increases in expression are useful for diagnostic or prognostic use." (Page 8 of the instant Office Action). In support of this assertion, the Examiner cites Hanna *et al.* to the effect that "the clinical significance of such results is unclear." Applicants respectfully point out that the quoted statement refers only to a particular type of results from a subset of tumors, in which protein overexpression is found without gene amplification, or a lack of protein overexpression is found with gene amplification. Gene amplification results themselves are clearly disclosed to be useful in disease prognosis and in predicting the response to various treatment regimens. For example, Hanna *et al.* notes that "HER-2/neu amplification in node negative patients can be used as an independent prognostic indicator for early recurrence, recurrent disease at any time and disease-related death. Demonstration of HER-2/neu gene amplification by FISH has also been shown to be of value in predicting response to chemotherapy in stage-2 breast cancer patients." (Page 1, col. 2). Hanna *et al.* further discloses that "patients with amplified HER-2/neu benefited from treatment with higher doses of adriamycin-based therapy, while those with normal HER-2/neu levels did not." (Page 1, col. 2). Thus, detection of gene amplification of HER-2/neu clearly has multiple prognostic uses.

The Examiner further cites Hyman *et al.* to the effect that "the utility of gene expression profiling in the identification of specific therapeutic targets remains limited." Applicants respectfully point out that Hyman *et al.* focus on results from gene amplification, not expression profiling, and the authors conclude that "gene amplification provides a powerful approach to highlight genes with an important role in cancer, as well as to prioritize and validate putative targets for therapeutic development. " (Page 6244, col. 2). Furthermore, Hyman *et al.* conducted

additional studies of one of the genes found to be amplified, HOXB7, and found "a clinical association between HOXB7 amplification and poor patient prognosis." (Page 6244, col.1 to col.2). Thus the results of Hyman *et al.* confirm that genes which are amplified in tumors have prognostic utility.

The Examiner also cites Pollack *et al.*, to the effect that multiple variations in gene copy number and expression "may contribute to the development or progression of cancer." The Examiner's attention is respectfully directed to the final paragraph of Pollack *et al.*, wherein the authors conclude that "a substantial portion of the phenotypic uniqueness (and, by extension, the heterogeneity in clinical behavior) among patients' tumors may be traceable to underlying variation in DNA copy number." (Page 12698, col. 2). Accordingly, genes that are amplified in at least one type of tumor are useful as markers for that type of tumor, and for prognostic uses directed to that type of tumor.

Applicants respectfully remind the Examiner that the correct test of utility is not absolute certaintly, but whether the utility is "more likely than not." The Patent Office has failed to meet its initial burden of proof that Applicant's claims of utility are not substantial or credible. Therefore, Applicants submit that the Examiner's reasoning is based on a misrepresentation of the scientific data presented in the above cited references and application of an improper, heightened legal standard. In fact, contrary to what the Examiner contends, the art, including the the results disclosed in Hanna *et al.*, Hyman *et al.*, and Pollack *et al.*, indicate that it is more likely than not that a gene which is amplified in tumor tissues is useful as a diagnostic or prognostic marker for cancer.

The Examiner asserts that "[b]ecause aneuploid DNA can be found in normal tissues, detection of increased DNA copy number does not necessarily mean those cells containing the DNA are cancerous." (Page 9 of the instant Office Action). In support of this assertion, the Examiner cites references by Fleischhacker *et al.* and Hittleman.

Applicants respectfully submit that Hittleman and Fleischhacker *et al.* do not disclose aneuploid DNA in "normal" tissue or cells, but in tissue that has been damaged by carcinogenic agents and is closely associated with tumorous tissue.

Applicants note that the title of the Hittleman paper is "Genetic Instabilities in Epithelial Tissues at Risk for Cancer." Hittleman studied lung tissue from chronic smokers, which had been exposed for years to carcinogenic tobacco smoke. As Hittleman explains, "[t]umors of the aerodigestive tract have been proposed to reflect a 'field cancerization' process whereby the whole tissue is exposed to carcinogenic insult (e.g., tobacco smoke) and is at increased risk for multistep tumor development (page 3). The detection of increases in chromosome number therefore identifies cells which have begun the first steps in this multistep progression to cancer. Even if these particular epithelial regions are not yet cancerous, their presence is strongly correlated with the development of cancer in the target tissue as a whole. Accordingly, Hittleman concludes that "the measurement of chromosome instability in the target tissue will be useful in assessing cancer risk as well as response to intervention" (page 10).

The Fleischhacker *et al.* paper presents a similar situation, in which pre-cancerous tissues having increased chromosome number are strongly correlated with cancer in the overall target tissue. Fleischhacker *et al.* studied colon samples that were themselves morphologically normal, but were derived from patients with colon cancer. Fleischhacker *et al.* suggest that "individuals with colon cancer may have morphologically normal colonic tissue, which is genetically abnormal, and this abnormality may precede the development of mutations in K-ras." (Abstract).

Accordingly, both Hittleman and Fleischhacker *et al.*, show that an increase in chromosome number or gene amplification is associated not with normal tissues, but with cancerous, or pre-cancerous tissues, and therefore, an increase in chromosome number or gene amplification is a useful marker for a cancerous or pre-cancerous state. Detection of pre-cancerous cells or tissues is useful because, as explained by Hittleman, it allows for assessing cancer risk, as well as response to intervention. Hence, Applicants respectfully submit that whether a pre-cancerous or tumor sample were analyzed, the showing of DNA amplification of the PRO1295 gene would still be significant, since it would lead to the diagnosis of either a pre-cancerous state or a cancerous state, which is the utility asserted here.

The Examiner asserts that "there is no indication that the cell lines typified are characterized with respect to vascularization or other morphology which is indicative of

progression or metastases and which may all exhibit changes in gene expression that may be non-diagnostic or prognostic in nature." (Page 9 of the instant Office Action).

Applicants respectfully submit that the specification clearly provides detailed information about the tumors used in the gene amplification assay, including information related to tumor progression or metastasis. For example, the lung cancer samples and cancer cell lines in the gene amplification assay represent different types, stages and physiological conditions of lung tumors. For example, on page 331, line 37 of the specification states, "The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8." Further, on page 337, line 9, the specification discloses that Table 8 describes "T stage and N stage of various primary tumors which were used to screen the PRO polypeptide compounds of the invention."

Applicants respectfully submit that lung cancer staging is the process of finding out how localized or widespread the cancer is. Each stage describes how far the cancer has spread. Treatment and prognosis depend on the cancer's stage.

The system used to describe the growth and spread of non-small cell lung cancer (NSCLC) in the instant application is the TNM staging system. T stands for tumor (its size and how far it has spread within the lung and to nearby organs), N stands for spread to lymph nodes, and M is for metastasis (spread to distant organs). In TNM staging, information about the tumor, lymph nodes, and metastasis is combined and a stage is assigned to specific TNM groupings. The grouped stages are described using the number 0 and Roman numerals from I to IV (1 to 4).

Accordingly, Table 7 also shows that these tested lung tumors and tumor cell lines are from various growth stages, such as IA, IIA, IIIA, IB, IIB, etc., or T1, T2, or T3, or N0, N1, or N2 stages.

Hence, Applicants submit that specification provides clear and detailed information about the tumors used in the gene amplification assay, including information relevant to progression and metastasis.

Finally, the Examiner asserts that "the claims are broadly drawn to hybridizing fragments and encoding variants which have nucleic acid substitutions exhibiting an unpredictable effect

upon the sequences related to that of SEQ ID NO:53. One skilled in the art would expect that such variant sequences would lose their specificity as probes for the target sequence." (Pages 10-11 of the instant Office Action).

Applicants first respectfully point out that the claims, as amended in the Response filed February 7, 2005, do not recite variant nucleic acid sequences encoding SEQ ID NO:54. The claims recite isolated nucleic acids comprising: the nucleic acid sequence of SEQ ID NO:53; the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:53; or the full-length coding sequence of the cDNA deposited under ATCC accession number 203287. Thus this aspect of the rejection is moot.

Applicants next respectfully point out that the claimed hybridizing fragments are fragments of SEQ ID NO:53 itself, or complements thereof. Hence, it would be obvious to one of skill in the art that these fragments of SEQ ID NO:53 could be used as specific probes for the target sequence of SEQ ID NO:53, from which they are derived. The claimed fragments therefore share the diagnostic and prognostic utilities of SEQ ID NO:53 itself.

Accordingly, Applicants have demonstrated a credible, specific and substantial asserted utility for the claimed polynucleotides. Further, based on this utility and the disclosure in the specification, one skilled in the art at the time the application was filed would know how to use the claimed polynucleotides.

In view of the above, Applicants respectfully submit that the specification discloses at least one credible, substantial and specific asserted utility for the PRO1295 polynucleotide and hybridizing fragments thereof. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejections under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph.

IV. Claim Rejections Under 35 U.S.C. §112, First Paragraph (Written Description)

Claims 33, 38-40, and 44-54 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the invention was filed, had possession of the claimed invention." (Pages 11-12 of the instant Office

Action). In particular, the Examiner asserts that the specification does not describe the claimed polynucleotides encoding the polypeptide of SEQ ID NO:54 and hybridizing fragments.

Applicants first respectfully point out that the claims, as amended in the Response filed February 7, 2005, do not recite variant nucleic acid sequences encoding SEQ ID NO:54. The claims recite isolated nucleic acids comprising: the nucleic acid sequence of SEQ ID NO:53; the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:53; or the full-length coding sequence of the cDNA deposited under ATCC accession number 203287. Thus this aspect of the rejection is moot.

The Examiner asserts that "while the specification and claims refer to Figure 32, no definitive direction is provided as to the coding region of SEQ ID NO:53." (Page 12 of the instant Office Action). Applicants respectfully point out that the claims do not refer to any Figures, and that it is Figure 31 which shows the nucleic acid sequence of SEQ ID NO:53. Figure 31 clearly identifies the start and stop codons, shown in bold and underlined, which delimit the coding region. This marking is clearly explained in the description of Figure 31 (page 286, lines 25-27). As the coding region of a gene is defined by the start and stop codons, one of skill in the art would immediately understand that the coding region of SEQ ID NO:53 is the sequence beginning with the start codon and ending with the stop codon.

With respect to the claimed hybridizing fragments, Applicants respectfully point out that these hybridizing fragments are fragments of SEQ ID NO:53 itself, or complements thereof. The Examiner acknowledges that SEQ ID NO:53 meets the written description provision of 35 U.S.C. §112, first paragraph. (Page 12 of the instant Office Action). Since SEQ ID NO:53 has been described, fragments of SEQ ID NO:53 (or complements thereof) are also described. The nucleic acid sequence of SEQ ID NO:53 has been provided as shown in Figure 31. One of skill in the art would readily recognize fragments of at least 20 to at least 100 nucleotides of SEQ ID NO:53. Listing every such fragment would be redundant, and would needlessly clutter the specification.

Accordingly, the specification provides adequate written description for the claimed hybridizing fragments of SEQ ID NO:53. For the above-noted reasons, Applicants respectfully

request the Examiner to reconsider and withdraw the written description rejections under 35 U.S.C. §112, first paragraph.

V. Claim Rejections Under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 33, 38-40, and 44-54 stand rejected under 35 U.S.C. §112, first paragraph, because allegedly "the specification does not reasonably provide enablement for the variable encoding and hybridizing sequences and for such generic sequences where no requisite functional activity is provided as claimed." (Page 14 of the instant Office Action).

Applicants respectfully disagree and traverse the rejection.

Applicants first respectfully point out that the claims, as amended in the Response filed February 7, 2005, do not recite variant nucleic acid sequences encoding SEQ ID NO:54. The claims recite isolated nucleic acids comprising: the nucleic acid sequence of SEQ ID NO:53; the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:53; or the full-length coding sequence of the cDNA deposited under ATCC accession number 203287. Thus this aspect of the rejection is moot.

Applicants next respectfully point out that the claimed hybridizing fragments are fragments of SEQ ID NO:53 itself, or complements thereof. Hence, it would be obvious to one of skill in the art that these fragments of SEQ ID NO:53 could be used as specific probes for the target sequence of SEQ ID NO:53, from which they are derived. The use of fragments of genes as hybridization probes is well known in the art, and is also disclosed in the specification at, for example, page 359, lines 15-26, and page 364, lines 25-38. Thus one of ordinary skill in the art would understand how to use the claimed fragments to detect SEQ ID NO:53, without any undue experimentation. Whether or not the claimed fragments are themselves amplified in human tumors is irrelevant, because the claimed fragments can clearly be used as probes to detect SEQ ID NO:53, which is known to be amplified in human tumors. The claimed fragments therefore share the diagnostic and prognostic utilities of SEQ ID NO:53 itself.

For the above-noted reasons, Applicants respectfully request the Examiner to reconsider and withdraw the enablement rejections under 35 U.S.C. §112, first paragraph.

VI. Claim Rejections Under 35 U.S.C. §102

Claims 48-54 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by GenEmbl Accession No. AC016400. The Examiner asserts that Accession No. AC061400 teaches a nucleic acid sequence corresponding with 100% sequence identity to residues 1509-2564 of SEQ ID NO:53. Applicants respectfully point out that this assertion appears to be incorrect. The longest contiguous segment of overlap between SEQ ID NO:53 and the reference sequence is only 167 nucleotides.

Applicants further respectfully note that the earliest publicly available date for Accession No. AC061400 is November 26, 1999. As discussed above, the pending claims of the instant application are entitled to the effective priority date of October 29, 1999; hence Accession No. AC061400 is not prior art under 35 U.S.C. §102(b) since its publication date is after the effective priority date of this application. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection under 35 U.S.C. §102(b).

CONCLUSION

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2830 P1C44**)

Respectfully submitted,

Date: July 19, 2005

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